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14. ABSTRACT
Prospect Theory (PT), with risk-attitudes, helps us understand decision-making under conditions of risk and can be applied to decisions regarding prostate cancer. Other models have suggested that risk-perceptions may better explain risky choices. The aim of this study was to assess the mechanism (risk-attitude vs. risk-perceptions) by which risky choices (preferences) are made. Risk-perceptions were assessed with a questionnaire and preferences were measured with the Time Trade-Off interview. 290 men, 144 with prostate cancer and 146 without, were randomized to either a loss or gain framed interview. Our hypothesis that the mechanism driving risky choice is a combination of risk-perceptions and risk-attitude was supported with the combination shown to be significantly associated with preferences. Our hypothesis related to the effect of message framing on preferences was supported only in part since there were no within group differences, however message framing did show modestly significant between group (patient versus community) differences for loss and gain frame related to impotence but not incontinence. This study also supports PT with patients willing to risk more side effects to gain longer survival than the community subjects.

15. SUBJECT TERMS
Prostate cancer, Decision making, TTO, Utilities, Risk perceptions

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A. Introduction:

This study evaluated two different populations, a community sample without prostate cancer, and a group of men diagnosed and treated for prostate cancer. The study was designed to evaluate the decision-making mechanism (i.e., risk-attitude versus risk-perceptions) and processes (i.e., cognitive versus affective) that influence their preferences for specific treatments (e.g., surgery and radiotherapy) and associated health states (i.e., sexual impotence and urinary incontinence). In order to assess risk-attitude versus risk-perception two variables were considered, the point of reference of the subject (i.e. person with prostate cancer versus person without prostate cancer) and the way the treatment alternatives are communicated or framed (loss-framed message versus gain-framed message).

B. Body:

Objectives:

Aim 1: The proposed study will assess the mechanism (risk-attitude versus risk-perceptions) by which preferences are made for health outcomes.

Aim 2: The proposed study will asses potential mediators of risk attitude/perceptions, stated preferences and calculated utilities by assessing cognitive-affective factors individuals may weigh in making risky choices through the quantitative Risk Perceptions Questionnaire (conducted as part of the current analyses) and the more qualitative Cognitive-Affective Mediating Units Questionnaire (to be analyzed in the future).

Aim 3: The proposed study will assess differences in risk-attitude/perceptions, cognitive-affective profile, stated preferences, and calculated utilities among the groups studied.

Background:

Expected Utility theory (EU) and its psychologically more accurate extension, Prospect Theory (PT), have recently moved from the realm of economic decision making into healthcare decision making. These theories underlie several cost-utility analyses (CUA) of prostate cancer (PC) showing little benefit relative to the cost of screening and treating asymptomatic men [1-3]. Population and health policy decisions regarding prostate cancer screening and treatment have recently been influenced by these studies which have been cited in National and State-wide debates over prostate cancer screening benefits [4, 5].

Current projections indicate that 198,100 new cases of PC will be diagnosed this year, and that 31,500 men will die of the disease [6]. Sensitive and reliable methods for the screening of PC exist, yet questions regarding the cost-effectiveness of screening and treatment have been raised [2, 7]. Most of the controversies center around the argument that screening only leads to the detection and costly treatment of latent tumors that would have remained clinically silent and only discovered on autopsy, while causing major

decrements in quality of life [8]. The CUA damning to PC screening were sensitive to assumptions regarding survival and *utilities*. Although results from large clinical trails are still pending [9], improved survival rates with screening have been suggested by others [10-12]. However, the use of utilities in health care decision making is under debate and many aspects are not yet fully understood. A utility is a value between 0 (death or worst possible health) and 1 (best possible health), used to weight survival or other health outcome. Utilities are derived from individual preferences. Preference can be defined as a subject's contemplative first choice among a series of risky alternatives. Recommendations for the use of CUA as a framework for assessing health care programs have been published [13].

One concern with the use of utilities is that it is possible to manipulate the values depending on the risk-message framing used to elicit preferences. Studies show that manipulation of message framing (as a loss or gain from a reference point) will frequently elicit a predictable risk–attitude (risk aversion for gains and risk seeking for losses) [14, 15]. However risk-attitude itself does not fully explain preferences/utilities and leaves us lacking necessary knowledge needed to improve risk message framing. Middle range theories such as the Risk-Return Model and the Cognitive-Affective Model of Decision Making have been used to better understand decision making under conditions of risk and risk message framing. But first, utilities and the preferences from which they are derived are best examined via the theoretical framework guiding their purpose and use in medical decision-making – Welfare Economics.

Welfare Economics - is concerned with the systematic assessment of the desirability, from a societal perspective, of alternative allocations of resources [16], or in other words, the achievement of a social maximum derived from individual desires [17]. A social maximum for a particular program can be derived from a variety of methods including the sum of individual utilities. Welfare Economics assumes that individuals maximize a preference function (utility) for material consumption (including health care), and that this preference follows certain conditions of rationality and logical consistency [16, 18]. It also assumes that the overall welfare of society is the sum of these individual preference/utility functions. Proponents believe, for the purpose of health policy, that Welfare Economics can lead, in most circumstances, to an efficient allocation of resources when the decisions (preferences) involved reflect a societal rather than an individual perspective [16, 18]. However from the clinical viewpoint it may be the patient perspective that is most valid [16, 18, 19].

An additional concept important to resource allocation is the "veil of ignorance". This concept holds that decisions of resource allocation should be made from behind the veil of ignorance of which position in life, rich or poor (*healthy or ill*) one will be born to or acquire. In this way the bias of personal advantage or disadvantage is removed from decision-making [20]. Individuals in a health state of interest or those who have a vested interested in a disease or therapy (e.g., physicians) would not be considered as decision-makers behind the veil of ignorance. However, there are those who argue that these biases cannot truly be removed [19] and the more informative issue would be to

understand how such biases impact preferences. To accomplish this, group differences in preferences and the decision making process driving them would need to be explicated.

The need to better understand the differences in preferences among groups is underscored by conflicting results from several studies showing subjects in a specific health state to have higher (more desirable) utilities for health states when they are in them versus subjects who are not [21], and studies showing just the opposite [22]. Other studies have shown patients and physicians having similar preferences for health states [21], and just the opposite with patients and physicians having significantly different preferences and utilities for the same health states [23]. In our own work we found PC patients to have no significant difference in preferences and utilities for health states related to therapy as compared to men at risk for but without the disease [24].

In summary, Welfare Economics guides the purpose and from which populations we should analyze preferences and utilities. However the preferences/utilities underpinning this framework are not fully understood. It is within this context that the middle range theories, Expected Utility Theory (EU) and Prospect (PT) found their impetus.

Utility-Based Choice Models: Expected Utility Theory (EU) is a normative theory (how decisions *should* be made) for decision making under conditions of uncertainty/risk. EU evolved as an explanation of how people should respond when making risky choices (gambling) between hypothetical monetary lotteries, although it has been argued that the axioms provide a strong foundation for health-related EU [25]. However flaws in the axioms indicating that human decision-making does not fully conform to expected EU have been well documented [26-30], most classically by Allais [31] Ellsberg [32].

Violations of EU as a normative theory may occur due to several perceptual processing characteristics used in decision-making including the fact that choices between gambles and certainty equivalents are distorted by the "certainty effect" [33, 34]. This effect has been explained in terms of Prospect Theory (PT), a competing descriptive theory (of how decisions *are* made). PT explains the certainty effect as the mechanism by which people tend to overweight outcomes with low probabilities and underweight outcomes with high probabilities [35]. PT suggests a non-linear utility or preference function to explain the certainty effect and another of the major violations of EU where by people avoid risks in the domain of gains and seek risks in the domain of losses relative to a change from their reference point. Kahneman & Tversky (K&T) (1979) proposed an S-shaped preference function that, relative to the reference level (the point of inflection), is concave in the domain of gains and convex in the domain of losses. This phenomenon has traditionally been associated with *risk attitude*, risk-aversion explaining the concavity and risk-seeking explaining the convexity.

Utility-Based Choice Models vs. Risk-Return Models of Preference: Risk-Attitude versus Risk Perceptions: The traditional focus on risk-attitude has not been able to satisfactorily explain risky choice behavior across different domains and situations [36]. According to Weber this may be attributed not to risk attitude instability, but to the inappropriate definition of risk-attitude in UBMs [37]. Traditional utility-based choice

models (UBM) such as EU and PT predict preference for risky options by the cognitive mechanisms of preference/utility functions that have particular curvatures, which is labeled risk attitude. Risk-attitude in the EU sense of the word has nothing to do, however, with people's emotional responses to perceived risk, i.e., their tendency to be attracted or repelled by alternatives perceived as risky. Weber and colleagues [38, 39] have argued convincingly that both cognitive and affective mechanisms combine to shape people's evaluations of the riskiness and benefits of risky choice alternatives and the tradeoff (labeled *perceived* risk-attitude) that people are willing to make between those two. Empirical research (summarized in Weber[40]) shows that when preferences differ as the result of individual, cultural, or situational differences, the variable that tends to be instrumental in predicting the difference in preferences is the *perception of risks*, rather than either the perception of returns (or benefits) or, the risk-return tradeoff (or *perceived* risk-attitude [vs. EU risk-attitude]). *Perceived* risk-attitude tends to be moderately negative (or *perceived* risk-averse) for most individuals in most situations and across a range of cultures [40].

Risk-perceptions and *perceived* risk-attitude are more cogently explained by psychological Risk-Return Models (RRM) as compared to UBMs. RRMs allow for the fact that people perceive risks differently across domains or situations, which will affect their preferences (making them *appear* either risk-seeking or risk-averse in the EU sense of the word). When one controls for these differences in perceived risk, however, attitude towards risk has been found to be quite stable for a given individual [40]. While differences in risk perception rather than differences in *perceived* risk-attitude drive differences in preference, for some individuals differences in preference are actually driven by differences in *perceived* risk-attitude. Since UBMs do not make any distinction between those two mechanisms (risk-perceptions and risk-attitude), they also can not differentiate between individuals who differ on one rather than the other dimension. The distinction is important, however, since risk-perception is driven by both cognitive and affective processes, whereas *perceived* risk-attitude is purely affect driven (vs. EU risk-attitude which is cognitively driven). Changing people's perceptions of risk vs. changing their *perceived* risk-attitudes (or their EU risk-attitude) thus calls for very different interventions. It is an empirical question (to be examined by the proposed research) whether the theoretical distinction between risk-perception and *perceived* risk-attitude made by the risk-return framework, which allows for both cognitive and affective processes to operate as specified by CAM, provides us with a better way of predicting prostate patient's preferences and explain differences in preferences than the traditional EU or PT approach with their cognitive definition of risk-attitude.

In further support of differences in risk perceptions versus either EU or *perceived* risk-attitude as the mechanism driving preferences, multiple studies have found both a cognitive and an affective component to risky decision making [41, 42]. In a study to evaluate two models of risk perception for financial and health risks (e.g., investing 80% of savings in the stock of a new medical research firm; living near a nuclear power station), Holtgrave &Weber (H&W) [38] found that a combination of cognitive [C] and affective [A] dimensions of risk perception explained most of the variance: the [C] perceived probability of neither loss nor gain *(pr[status quo])*, the [C] perceived

probability of harm *(pr[harm])*, the [A] conditional expected value or amount of harm *(E[harm])*, [A] the degree to which the negative consequences of the activity/event are dreaded (*dread)*, the [C] perceived probability of *benefit (pr[benefit])*, and the [A] conditional expected value or amount of benefit *(E[benefit])* [38]. Although H&W originally labeled E[harm] and E[benefit] as cognitive factors, after lengthy consideration and in consultation with Dr. Weber, these factors are here labeled 'affective'. The strong emotional overtones of expectancies and values are more in keeping with the affective label and are more congruent with CAM [43]. This hypothesis will be tested in the future as part of our specific aims (AIM 2) in which we will look at associations among CAM cognitive-affective variables and the cognitive-affective variables as defined by Weber.

These studies support the hypothesis that a cognitive-affective process, labeled risk-perceptions, as defined by the RRM, rather than either the cognitive risk-attitude, as defined by UBM, or the affective *perceived* risk-attitude as defined by RRM, alone, is the more plausible mechanism driving risky decision making/preferences. However, this has not formally been tested in decision-making regarding cancer screening and treatment in general or PC screening and treatment in particular.

This study has begun to examine the mechanism (RRMs' risk-perceptions vs UBMs' risk-attitude) and mediating factors (cognitive and affective) involved in the decision making process of risky choices (preferences/utilities). The ultimate goal of this understanding would be to improve message framing and risk communications, which under controlled conditions, has been shown to improve risk perceptions [48].

<u>Methods:</u>

Eligibility for this study included men between 40 to 80 years of age. For the patient population, men diagnosed and treated for prostate cancer with either surgery or radiotherapy between 1 and 4 years prior to study were eligible. Patients were recruited with IRB approval and the permission of the participating physicians. The community sample was recruited through a wide variety of methods but the most successful strategy for community recruitment was radio advertisements. The community sample included men age 40 to 80 years of age without a history of prostate cancer.

Risk Perception Questionnaire: Based on the methodology described by Weber et al on risk perceptions and decision making [38, 39] the Risk Perception Questionnaire (Patient and Control versions) was developed (in consultation with Dr. Weber) to assess the dimensions of risk perception found to be the best predictors of decision making under conditions of PC and treatment-related health state risks. This includes the six cognitive [C] and affective [A] dimensions: the [C] perceived probability of neither loss nor gain *(pr[status quo])*, the [C] perceived probability of harm *(pr[harm])*, the [A] conditional expected value or amount of harm *(E[harm])*, [A] the degree to which the negative consequences of the activity/event are dreaded (*dread)*, the [C] perceived probability of *benefit (pr[benefit])*, and the [A] conditional expected value or amount of benefit *(E[benefit])* [38]. Subjects were asked to rate (state a preference for) a set of risky events with respect to each of the six dimensions on a 0 through 100 scale. The risky event questions are designed in tandem with the TTO questions to assess the decision-

making process involved in each trade-off. Subjects write their numeric response on a blank line. As in Weber's previous work, terms such as "benefits", "harm", and "risk" are intentionally left undefined or vague for the subject to interpret as he thinks best.

Using each of the six cognitive-affective dimensions described above, subscales were constructed to assess risk perceptions related to surgery and radiotherapy and the two most common symptoms associated with treatments, impotence and incontinence. Five subscales were developed to assess risk perceptions (RP) for the following constructs: being diagnosed with prostate cancer (subscale A) (RPA), being treated with surgery (subscale B) (RPB), being treated with radiation therapy (subscale C) (RPC), facing varying risks of incontinence (subscale D) (RPD), and facing varying risks of impotence (subscale E) (RPE). For conceptual congruity with the utility scores, RP item scores were recoded as needed so that 0 reflected worst outcome and 100 best outcome.

Time Trade-Off (TTO). The TTO derives a utility value from the point at which a person is indifferent between time x in better health and time y in some longer state of chronic illness [56]. The TTO adheres to utility theory [16, 57], and is the most common method of utility assessment used in PC [24]. TTO interviews were conducted asking subjects first to express their preferences among a series of treatment options (labeled Treatment A and B) and outcomes. In this particular study we compared Treatment A - surgery (radical prostatectomy) to Treatment B - RT (external beam). Some experts believe that therapies should not be named so as to avoid biases (from the labeling effect) in favor or against treatment options received or rejected by those with cancer, or feared by those without cancer. We, on the other hand, have found two flaws in this thinking through our past work: 1) the majority of men (even those without disease) are able to guess which therapy we are describing by the common scenarios needed to setup the tradeoffs, and 2) through a phenomenon we have labeled the "just cut it out" mentality, men appear to have a utility for surgery separate from any associated decrements in health states [24]. We therefore conducted a second series of treatment-labeled tradeoffs to follow the unlabeled series in a subset of subjects, to assess differences from the labeled series. We will conduct this subset analysis in the future.

Men in each group were randomized to either the loss-frame scenarios or the gain-frame scenarios. The interviews would have been prohibitively confusing and exhaustive for each participant to be subjected to a full series of loss followed by gain-framed trade-offs. An example of a loss-frame TTO question would be: "Which would you prefer, 5 years of life after Treatment A that leaves you with an 80% chance of losing your ability to have an erection and a 30% chance of losing control of your urine or living 4-1/2 years after Treatment B that leaves you with a 40% chance of losing your ability to have an erection and a 10% chance of losing control of your urine?" An example of a gain-frame question would be: "Which would you prefer, living 5 years of life after Treatment A that gives you a 20% chance of keeping your ability to have an erection and a 70% chance of keeping control of your urine or living 4-1/2 years after Treatment B that gives you a 60% chance of keeping your ability to have an erection and a 90% chance of keeping control of your urine?" Survival with the arbitrarily chosen reference state, Treatment B (RT), is offered in successively shorter increments of time until the subject

is indifferent to the trade (at which point the interview is concluded). For this study, the probabilities associated with the health states used in the TTO interviews were derived from an extensive review of the literature and reviewed by a urologist and radiation oncologist (and discussed in detail elsewhere, [24], and were as follows: impotence associated with surgery 0.8 and with RT 0.4; incontinence associated with surgery 0.3 and with RT 0.1. Also for this study the time horizon of the trade-off was 16 years. We have used 5 and 7 years in past studies. For this study we asked all participants to imagine they were 65 years old when they were making the trade-offs. This meant they would have a average life expectancy of 16 years with which to trade.

Utility values are calculated from stated preferences by converting the units of time into a decimal scale ranging between 0 to 1. For example, a subject who states he would trade-off one year of a 5 year survival in favor of a therapy with 40% chance of impotence and 10% chance of incontinence in order to avoid higher risks of adverse events with an alternative therapy (80% chance of impotence and a 30% chance of incontinence), would have a utility value of 0.80 for the therapy with the greater risk of impotence and incontinence. Utility values were obtained by converting the units of time into a decimal scale ranging between 0 and 1. For example, a subject who is indifferent between living 4 1/2 years after a therapy that leaves them with entire sexual function intact, and living 5 years after a therapy that leaves them with certain impotence, has a utility for the therapy associated with impotence of 4.5/5.0 or 0.9. With the Scenario TTO the question more closely mirrors reality and is actually "how much time would you trade to <u>*avoid*</u> *the risk* of a poor health state associated with a particular treatment?" Scenarios set up to avoid a poor health state actually assess the *Dis*utility a subject has for the health state associated with a particular treatment. However, since the language of decision-making science is Utility and not *Dis*utility the calculation must provide a TTO utility.

A scenario TTO utility, therefore, is calculated at the point a subject is indifferent between living (y-x) years having avoided a poor health state (by rejecting a particular treatment) and a longer time y at risk for the poor health state (associated with having accepted a particular treatment). The units here are in years; to convert them to conventional (0-1) utilities they are divided by the time horizon y. The calculation is as follows:

$$(y-x)/y = 1- (1/y)(x)$$

For example, in a scenario with a 5-year average life expectancy (y=5), where a subject states that he would be willing to give up 6 months (or x=0.5 years) of those life years to avoid an 80% chance of impotence associated with a particular treatment, the calculation is as follows:

$$\begin{aligned}(5-.5)/5 &= 1 - .2(.5)\\ &= 0.9\end{aligned}$$

Preference for individual treatments was determined by the arbitrary cut-off of awarding the preference to the therapy with a utility value of $\geq$ 0.6 as compared to observation.

C. Key Research Accomplishments:

1. List of untoward events that have occurred in the past year in connection with the project - None

2. Changes of Risk Factors(s) for patients (s) - None

3. Number of Participants Interviewed or seen since the last review - 2

4. Give number of additional participants needed in coming year – The total sample size for the study was 300, 150 patients with cancer and 150 community participants.

Year 1 2003		Year 2 2004		Year 3 2005	
Patients	**Community**	**Patients**	**Community**	**Patients**	**Community**
83	**9**	**65**	**141**	**2**	**0**
92		**206**		**2**	

5. Description of any changes in the protocol since date of last review - None

6. Clean copy of consent form (no stamp on consent form) – N/A

7. If protocol has been terminated, indicate reason and date, whether work was completed, and if not, why work was not completed - Protocol was terminated when it met accrual.

D. Reportable Outcomes of Study:

- Subject characteristics are presented in Table 1.
- There were sociodemographic differences between the patient and community samples but there were no significant differences between loss and gain frame arms within patient groups.
- Patients were almost 10 years older than the community sample. The younger community sample had a higher percentage of college graduates and were more likely to be employed than the patient sample.

Table 1. Subject Characteristics – Means (SD) or N and Frequencies (%): N=290

	Patient N=144		**Community N=146**	
	Loss Frame N=71	Gain Frame N=73	Loss Frame N=71	Gain Frame N=75
Age in years pt vs community*	67 (SD 7.74) Range 51-79		58 (SD 10.63) Range 40-78	
Age in years within group by gain vs loss frame	68 (SD 7.46) Range 51-79	66 (SD 7.88) Range 51-79	57 (SD 10.41) Range 40-77	57 (SD 10.91) Range 40-78

Ethnicity pt vs community White Black Other	128 (89%) 15 (10%) 1 (1%)		139 (95%) 6 (4%) 1 (1%)	
Ethnicity within group by gain vs loss frame White Black Other	62 (87%) 8 (11%) 1 (2%)	66 (90%) 7 (10%) 0	68 (96%) 2 (3%) 1 (1%)	71 (95%) 4 (5%) 0
Education pt vs community^ ≤ High School (HS) HS to ≤ College ≥Post Graduate	38 (26%) 76 (53%) 30 (21%)		15 (11%) 98 (71%) 33 (23%)	
Education within group by gain vs. loss frame ≤ High School (HS) HS to ≤ College ≥Post Graduate	20 (29%) 33 (46%) 18 (25%)	18 (25%) 43 (59%) 12 (16%)	11 (16%) 43 (60%) 17 (24%)	4 (5%) 55 (74%) 16 (21%)
Household Income before taxes last year pt vs community# ≤ $29,999 $30,000 - $74,999 ≥$75,000 Refused	18 (13%) 57 (39%) 46 (32%) 23 (16%)		12 (8%) 52 (36%) 67 (46%) 15 (10%)	
Household Income within group by gain vs loss frame ≤ $29,999 $30,000 - $74,999 ≥$75,000 Refused	8 (13%) 24 (34%) 23 (32%) 15 (21%)	9 (13%) 33 (45%) 23 (31%) 8 (11%)	6 (8%) 26 (47%) 29 (41%) 10 (14%)	6 (8%) 26 (35%) 38 (50%) 5 (7%)
Marital Status pt vs community Married	110 (76%)		113 (77%)	

Not Married	34 (24%)		33 (23%)	
Marital Status within group by gain vs loss frame Married Not Married	 55 (77%) 16 (23%)	 55 (75%) 18 (25%)	 60 (85%) 11 (15%)	 53 (71%) 22 (29%)
Work Status pt vs community¥ Working (FT /PT) Not Working	 63 (44%) 81 (56%)		 93 (64%) 53 (36%)	
Work Status within group by gain vs loss frame Working (FT /PT) Not Working	 30 (42%) 41 (58%)	 33 (45%) 40 (55%)	 43 (61%) 28 (39%)	 50 (67%) 25 (33%)

*nonparametric Wilcoxon p-value p<.0001; ^Chi-square p-value p<.01; #Chi-square p-value p<.03; ¥Chi-square p-value p<.0001

- Table 2 illustrates that there are no significant within group (patient or community) differences in utilities for any risk of impotence or incontinence by loss or gain frame.
- There are modestly significant between group (patient versus community) differences for loss frame related to impotence but no significant between group difference related to incontinence.
- There are highly significant between group (patient versus community) differences for gain frame related to impotence but no significant between group differences related to incontinence.

Table 2. TTO Utilities (Mean and Standard Deviations) for 16-Yr Survival with Treatments Associated with Varying Probabilities of Symptoms versus Less Survival with Observation but No Treatment Related Symptoms

	Patient N=144		**Community N=146**		
	Loss Frame N=71	Gain Frame N=73	Loss Frame N=71	Gain Frame N=75	t-test p-value
Incontinence					
10% Risk between groups	0.95 (0.11)		0.92 (0.18)		0.09
10% Risk within groups	0.95 (0.12)	0.96 (0.10)	0.92 (0.20)	0.93 (0.16)	NS
20% Risk between groups	0.93 (0.13)		0.90 (0.19)		0.12
20% Risk within groups	0.92 (0.13)	0.93 (0.13)	0.90 (0.20)	0.90 (0.17)	NS
25% Risk	0.90 (0.17)		0.88 (0.19)		0.39

between groups					
25% Risk within groups	0.88 (0.12)	0.91 (0.15)	0.88 (0.21)	0.88 (0.18)	NS
Impotence					
30% Risk between groups	0.95 (0.11)		0.89 (0.16)		**0.0005**
30% Risk within groups	0.94 (0.13)	0.96 (0.08)	0.89 (0.19)	0.90 (0.13)	NS
45% Risk between groups	0.92 (0.14)		0.85 (0.18)		**0.0007**
45% Risk within groups	0.92 (0.16)	0.92 (0.12)	0.87 (0.20)	0.82 (0.16)	NS
60% Risk between groups	0.90 (0.15)		0.83 (0.19)		**0.0002**
60% Risk within groups	0.90 (0.16)	0.90 (0.14)	0.84 (0.21)	0.82 (0.17)	NS

- Table 3 shows the results of the multivariate analyses to assess predictors of preferences for treatment-related side effects for prostate cancer. The following variables were entered into the model; group, age, ethnicity, education, marital status, and each of the risk perception subscale sores A through E.
- For incontinence at any level of risk tested (10%, 20%, 25%), there was a weak association with ethnicity, with Caucasians having a higher utility for incontinence than other ethnicities.
- Risk perceptions as measured by the risk perceptions (RP) questionnaire using the bladder-related subscale (subscale D) (RPD) showed that having a higher score, meaning perceiving bladder-related issues to be of less risk for interfering with one's life, was associated with higher utility for bladder-related symptoms. This was unrelated to age, education or marital status or whether we asked men with or without prostate cancer. This was also unrelated to the other RP subscales including being diagnosed with prostate cancer (subscale A) (RPA), being treated with surgery (subscale B) (RPB), being treated with radiation therapy (subscale C) (RPC), or facing varying risks of impotence (subscale E) (RPE).
- For impotence at all levels of risk tested (30%, 45%, 60%), patients had a significantly higher utility for this symptom compared to the community sample. Risk perceptions as measured by the risk perceptions (RP) questionnaire using the radiation therapy subscale (subscale C) (RPC) were negatively associated with utility scores, meaning the more subjects perceived having radiotherapy as negatively impacting their lives the more they showed a tolerance for impotence. The bladder-related subscale (subscale D) (RPD) showed that having a higher score, meaning perceiving bladder-related issues to be of less risk for interfering with one's life, was associated with higher utility for incontinence. This was unrelated to age, education or marital status or to risk perceptions related to being diagnosed with prostate cancer (subscale A) (RPA) or being treated with surgery

(subscale B) (RPB). For a 45% and 60% risk of impotence how subjects perceived erectile dysfunction impacting their life as measured by the sexual function-related subscale (subscale E) (RPE), also was associated with their preferences. Again higher risk perceptions scores were associated with higher utility scores.

Table 3. Stepwise Multivariate Regression Models for Predictors of Preferences for Treatment Alternatives with Attendant Risks of Impotence and Incontinence

Variable	**Parameter Estimate + SE**	**R^2**	**F**	**p-value**
Incontinence				
10% risk		**.064**		
Intercept	0.712 (0.06)		126.62	<.0001
Ethnic (White)	0.064 (0.04)		2.23	0.14
RPD	0.0002 (<0.001)		15.03	0.0001
20% risk		**.080**		
Intercept	0.644 (0.07)		96.08	<0.0001
Ethnic (White)	0.083 (0.05)		3.46	0.06
RPD	0.0003 (<0.001)		18.73	<0.0001
25% risk		**.084**		
Intercept	0.585 (0.07)		68.76	<0.0001
Ethnic (White)	0.10 (0.05)		4.38	0.04
RPD	0.0003 (<0.001)		18.98	<0.0001
Impotence				
30% risk		**.102**		
Intercept	0.803 (0.04)		417.98	<0.0001
Patient	0.069 (0.02)		13.76	0.0003
RPC	-0.0001 (<0.0001)		2.89	0.09

RPD	0.0002 (<0.0001)		15.25	0.0001
45% risk		**.105**		
Intercept	0.736 (0.05)		231.31	<0.0001
Patient	0.07 (0.02)		10.03	0.0017
RPC	-0.0002 (0.0001)		4.40	0.04
RPD	0.0002 (<0.0001)		5.29	0.02
RPE	0.0002 (<0.0001)		6.59	0.01
60% risk		**.118**		
Intercept	0.708 (0.05)		195.45	<0.0001
Patient	0.072 (0.02)		9.91	0.0019
RPC	-0.0002 (0.0001)		5.30	0.02
RPD	0.0001 (<0.0001)		2.89	0.09
RPE	0.0002 (<0.0001)		12.15	0.0006

Note: All variables left in the model are significant at the 0.1500 level.

E. Conclusions: In a sample of 290 men, 144 patients (mean age 67) with prostate cancer and 146 community subjects (mean age 58) without prostate cancer, subjects were randomized to a loss or gain message-framed measure of preference and utility for health states related to prostate cancer. Our preliminary analysis supports our hypothesis that the mechanism driving risky choice is a combination of risk-perceptions and risk-attitude, rather than the traditional concept of EU risk-attitude alone. This is demonstrated in the multivariate analyses where risk perceptions were shown to be significantly associated with preferences and utility values for prostate cancer therapies and treatment related side-effects. Our hypothesis related to the effect of message framing on preferences was supported only in part. Message framing had no effect on preferences among patient groups or among community groups, however message framing did show modestly significant between group (patient versus community) differences for loss frame and for gain frame related to impotence but no significant between group difference for message framing related to incontinence.

This study also supports Prospect Theory (PT) which suggests that people avoid risks in the domain of gains and seek risks in the domain of losses relative to a change from their reference point. Kahneman & Tversky (K&T) (1979) proposed an S-shaped preference function that, relative to the reference level (the point of inflection), is concave in the domain of gains and convex in the domain of losses. This phenomenon has traditionally been associated with *risk attitude*, risk-aversion explaining the concavity and risk-seeking explaining the convexity. The current study supports this with the findings that patients have higher utilities for treatment options and associated side-effects than the community subjects. This means that patients, as we hypothesized based on PT, were more risk-seeking (would risk more side effects to gain longer survival) than the community subjects who were more risk-averse in their gambles.

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G. Appendices: None at this time.